REMARKS

Claims 40 and 48 have been cancelled without prejudice for pursuit in a continuation application. Claims 1, 2, 5, 8, 10, 11-13, and 42, as amended, and claims 3, 4, 7, 9, 39, 41, and 43 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 10, line 5. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejection of claims 1-5, 7-13, and 39-43 under 35 U.S.C. § 101

The Office Action maintains the rejection of claims 1-5, 7-13, and 39-43 under 35 U.S.C. § 101 as being directed to an invention having no apparent substantial utility. Specifically, the Action states that the as-filed specification does not describe a substantial utility for any of the claimed sequences. The Action, however, acknowledges at page 3 that the as-filed specification does describe both a specific and credible utility for the claimed sequences.

Applicants respectfully disagree with the Action's assertion that the as-filed specification does not describe a substantial utility for any of the claimed sequences. As discussed in Applicants' response to the Office Action mailed April 8, 2003, the instant application teaches:

- that FGF-like mRNA expression is found primarily in the liver (page 4, line 39 to page 5, line 1; page 80, lines 14-16; and page 81, lines 2-5),
- the structural similarity of FGF-like polypeptide to members of the FGF family (Figures 3A-3D), and
- the likelihood that FGF-like polypeptide is secreted into the bloodstream where it may exert effects on distal sites (page 5, lines 5-7; page 77, line 27 to page 78, line 1; and page 79, lines 22-25). In view of this disclosure of *experimental results* obtained for the claimed nucleic acids, Applicants specifically assert in the specification that the FGF-like molecules of the present invention may be useful for, *inter alia*, regulating cells within or near the liver or regulating intestinal cell activity (page 2, lines 20-21; page 2, line 29 to page 3, line 1; page 3, lines 8-9 and lines 26-28; and page 5, lines 7-9). More importantly, the instant application further teaches a specific phenotype expressed by transgenic mice expressing an FGF-like transgene of the invention (page 4, lines 22-

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28). Specifically, transgenic mice expressing an FGF-like transgene exhibit an abnormal phenotype generally characterized as inhibited or delayed maturation, including reduced body weight, reduced liver weight as a percent of body weight, reduced spleen weight as percent of body weight, increased thymic weight as percent of body weight, and poorly developed ovaries with lack of significant follicular development. Applicants contend that a skilled artisan would recognize, in view of this explicit disclosure, that polypeptides encoded by the claimed sequences could be useful, for example, as growth or fat deposition inhibitors (page 5, lines 15-16) or in the treatment or prevention of liver-related diseases and disorders (page 5, lines 23-25 and page 76, lines 4-5).

Applicants contend that in view of the teachings of the instant specification described above, the claimed polypeptides would have substantial real world use as, for example, regulators of liver cell growth, an assertion that was *explicitly* made in the specification. In addition, the asserted uses are substantial because they have "real world" effects, *inter alia*, causing reduced body weight. Applicants will now address each of the Action's individual assertions as to this ground of rejection below:

a. The specification need not describe the specific biological function of the disclosed FGF-like polypeptides

The Action asserts that the specification does not describe a substantial utility for any of the claimed sequences because the specification fails to describe the *specific biological function* of the disclosed FGF-like polypeptides (*i.e.*, the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4). Specifically, the Action states that specification fails to describe the specific ligands that interact with the disclosed FGF-like polypeptides or a well-established biological pathway in which the disclosed FGF-like polypeptides participate. In addition, the Action states that such information is *essential*, in that that a skilled artisan requires such information in order to use any of the claimed nucleic acid molecules without any further investigation.

Applicants respectfully disagree with the Action's assertion that to satisfy the requirements of 35 U.S.C. § 101, Applicants have the burden of establishing that the as-filed specification describes the *specific biological function* of the FGF-like polypeptides encoded by the claimed nucleic acid molecules. As discussed in Applicants' response to the Office Action mailed April 8, 2003, the

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appropriate test for determining whether the claimed invention has patentable utility is provided by the *Utility Examination Guidelines*, which state that to satisfy the utility requirements of 35 U.S.C. §§ 101 and 112, first paragraph, Applicants' disclosure must contain an assertion of a specific and substantial utility that is credible. *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1098 (2001). Applicants contend, therefore, that the as-filed specification need not describe the specific ligands that interact with the disclosed FGF-like polypeptides or a well-established biological pathway in which the disclosed FGF-like polypeptides participate in order to satisfy the substantial utility prong. Indeed, because the disclosed FGF-like polypeptides share structural similarity with non-receptor members of the FGF family and are themselves secreted proteins, one of ordinary skill in the art would understand that the disclosed FGF-like polypeptides are likely to be ligands.

b. Applicants are not relying on post-filed evidence

The Action asserts that Applicants, in their response to the Office Action mailed April 8, 2003, relied on post-filed evidence to support their argument that the as-filed specification complies with 35 U.S.C. § 101.

Applicants are well aware that "the [claimed] invention [must] have a specific, substantial, and credible utility that would have been recognized by one of skill in the art *at the time the application was filed*," *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1094 (2001) (emphasis added), and therefore respectfully disagree with the Action's assertion they have relied on post-filed evidence to support their argument that the as-filed specification complies with 35 U.S.C. § 101. Applicants contend, instead, that the post-filed evidence to which the Action refers was *not* presented by Applicants to *establish* that the claimed invention has patentable utility, but rather to *confirm* that Applicants' assertion of utility in the instant application was *credible*. Applicants note that the portion of their response to the Office Action mailed April 8, 2003 citing the Strausberg and Nishimura *et al.* references addresses *only* the third prong of a proper utility analysis: *credible* utility. These references merely illustrate that those of ordinary skill in the art reached an identical conclusion concerning the identity of the claimed nucleotide sequences (albeit after Applicants' priority filing date of September 7, 1999), despite the fact that these skilled artisans knew *even less* about the claimed nucleotide sequences than Applicants (*e.g.*, neither Stausberg nor Nishimura

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performed transgenic mice experiments to identify a phenotype related to the overexpression of FGF-like polypeptides). In other words, the question of what those of ordinary skill in the art *would have or could have* understood from Applicants' disclosure has been answered by the art: Applicants' claimed nucleic acid encodes an FGF. Nevertheless, in view of the fact that the Strausberg and Nishimura *et al.* references were presented *only* on the issue of whether Applicants asserted a credible utility for the claimed invention, and further, in view of the Action's acknowledgement at page 3 that the as-filed specification describes a credible utility for the claimed sequences, Applicants contend that the issue of whether Applicants are relying on post-filed evidence is merely a red herring that distracts rather than focuses the remaining issue of whether Applicants have asserted a substantial utility for the claimed invention.

c. The specification need not describe only proven utilities for the disclosed FGF-like molecules

The Action asserts that because the as-filed specification recites a "laundry list" of utilities, some of which are not even related or are even contradictory to one another, the specification does not describe a substantial utility for any of the claimed sequences.

Applicants note that the present Action (as well as each of the prior Actions regarding the instant application) focuses much attention on the list of possible activities for the disclosed FGF-like molecules listed in the specification at page 5, line 6 to page 6, line 2. Applicants contend that one of ordinary skill in the art would recognize that this list merely enumerates a number of the activities possessed by members of the FGF family of proteins, and that a skilled artisan would recognize the particular activities possessed by the disclosed FGF-like molecules in view of the *actual experimental results* described in the specification. Specifically, Applicants contend that the specification's teachings regarding the expression of FGF-like mRNA in the liver (page 4, line 39 to page 5, line 1; page 80, lines 14-16; and page 81, lines 2-5), the secretion of FGF-like polypeptide into the bloodstream (page 5, lines 5-7; page 77, line 27 to page 78, line 1; and page 79, lines 22-25), and the abnormal phenotype associated with the overexpression of an FGF-like transgene in transgenic mice (page 4, lines 22-28) would readily inform a skilled artisan as to which of the FGF protein functions listed in the specification FGF-like polypeptides would share.

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Moreover, Applicants contend that the fact that the FGF-like molecules contemplated by the instant application could be used, for example, to *both* promote and inhibit cell growth (*i.e.*, the instant application contemplates both FGF-like polypeptide agonists and antagonists) negates the Action's assertion that the lack of relatedness of the listed activities is relevant to a substantial utility analysis. In addition, Applicants contend that the Action provides no support for requiring Applicants to recite only proven utilities for the disclosed FGF-like molecules, particularly in view of the fact that the *Utility Examination Guidelines* were published nearly sixteen months *after* the instant application was filed. However, in order to expedite prosecution of the pending claims to allowance, and in Applicants' view because it will have no substantive effect in the proper scope of the pending claims, Applicants would be willing to delete the activities listed in the specification at page 5, line 6 to page 6, line 2 to which the Examiner objects.

d. The specification provides support for using the disclosed FGF-like molecules as fat deposition inhibitors or as therapeutic agents for treating liver-related diseases

The Action asserts that neither the specification nor the results obtained with transgenic mice provide support for using the disclosed FGF-like molecules as fat deposition inhibitors or for treating a generalized liver-related disease or disorder.

Applicants respectfully disagree with the Action's assertion that the specification does not provide support for using the disclosed FGF-like molecules as fat deposition inhibitors or for treating a generalized liver-related disease or disorder. Applicants contend that one of ordinary skill in the art would readily recognize that polypeptides encoded by the claimed nucleic acid molecules could be useful as either growth or fat deposition inhibitors or in the treatment or prevention of liver-related diseases and disorders in view of the specification's teachings regarding the expression of FGF-like mRNA in the liver (page 4, line 39 to page 5, line 1; page 80, lines 14-16; and page 81, lines 2-5), the secretion of FGF-like polypeptide into the bloodstream (page 5, lines 5-7; page 77, line 27 to page 78, line 1; and page 79, lines 22-25), and the observation that transgenic mice expressing an FGF-like transgene exhibit an abnormal phenotype generally characterized as inhibited or delayed maturation, including reduced body weight, reduced liver weight as a percent of body weight, reduced spleen weight as percent of body weight, increased thymic weight as percent of body weight,

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and poorly developed ovaries with lack of significant follicular development (page 4, lines 22-28).

e. Applicants are not asserting that the making of a transgenic mouse expressing an FGF-like polypeptide is a substantial utility

The Action asserts that the making of transgenic mice expressing any of the claimed nucleic acid molecules is one of the "distinct and contrary . . . potential utilities" about which the "specification as a whole clearly generalizes and merely speculates." In addition, the Action asserts that because a skilled artisan would not have recognized that such transgenic mice were immediately useful for other than further investigation and research, the specification does not describe a substantial utility for any of the claimed sequences.

Applicants respectfully disagree with the Action's assertion that the asserted utility for the claimed FGF-like polypeptides is making a transgenic mouse that expresses an FGF-like transgene. Applicants provided an art-recognized example of determining a phenotype associated with a novel nucleic acid: showing the effect of overexpressing the nucleic acid in a cell or animal and detecting the effect. This – *not the mere creation of a transgenic mouse* – was the intent and effect of the cited disclosure, as would be recognized by anyone having ordinary skill in the art.

f. The transgenic mouse phenotype described in the specification is relevant to Applicants' assertion of utility

The Action asserts that the inhibited or delayed maturation phenotype described in the specification for transgenic mice expressing an FGF-like transgene is not evidence of a substantial utility for any of the claimed sequences, since the FGF-like transgene was "artificially over-expressed" in a "researched . . . and genetically engineered" animal that Applicants did not contemplate as a subject for any of the therapeutic utilities recited in the specification. The specification states that, at best, the transgenic mice serve merely as a research model, to be further investigated.

As discussed above, the instant specification describes *actual experimental results* using an *art-recognized* method for determining the phenotype associated with a novel nucleic acid, namely, the creation of a transgenic mouse. Specifically, the instant specification teaches that transgenic

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mice expressing an FGF-like transgene exhibit an abnormal phenotype generally characterized as inhibited or delayed maturation, including reduced body weight, reduced liver weight as a percent of body weight, reduced spleen weight as percent of body weight, increased thymic weight as percent of body weight, and poorly developed ovaries with lack of significant follicular development (page 4, lines 22-28). Applicants contend that one of ordinary skill in the art would appreciate that the results of the transgenic mice experiments described in the specification are *absolutely relevant* to the issue of whether the instant specification describes a substantial utility for any of the claimed sequences.

g. Structural similarity between the claimed nucleic acid molecules and members of the FGF protein family is not the sole basis for Applicants' assertion of utility

The Action asserts that because the "only main basis or nexus" for Applicants' assertion of utility is the similarity between the claimed nucleic acid molecules and those encoding FGF-4 and FGF-6, the specification does not describe a substantial utility for any of the claimed sequences.

Applicants respectfully disagree with the Action's assertion that the "only main basis or nexus" of Applicants' assertion of utility is the structural similarity between the claimed nucleic acid molecules and members of the FGF family of proteins (*i.e.*, that Applicants' assertion of utility is based *solely* on the structural similarity of the disclosed FGF-like polypeptides to members of the FGF family). On the contrary, as described above, the instant application discloses an *explicit example* of a biological function for the protein product of the claimed nucleic acid. Specifically, the instant application discloses that 6-8 week old transgenic mice that overexpressed an FGF-like transgene exhibited an abnormal phenotype generally characterized as inhibited or delayed maturation, including reduced body weight, reduced liver weight as a percent of body weight, reduced spleen weight as percent of body weight, increased thymic weight as percent of body weight, and poorly developed ovaries with lack of significant follicular development (page 4, lines 22-28). This was *not* a prophetic example, and was *not* a speculative function or utility. Rather, this disclosure provided a phenotype associated with overexpression of the claimed nucleic acid. It was also *not* based *solely* on structural similarity. In addition, Applicants note that the instant specification teaches that FGF-like mRNA expression is found primarily in the liver (page 4, line 39 to page 5, line 1; page 80, lines 14-16; and page 81, lines 2-5) and the likelihood that FGF-like

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polypeptide is secreted into the bloodstream where it may exert effects on distal sites (page 5, lines 5-7; page 77, line 27 to page 78, line 1; and page 79, lines 22-25). Based on the totality of the biological evidence presented in the as-field specification, Applicants contend that the asserted utility of the claimed polypeptides rests on *more* than their structural similarity to members of the FGF family.

h. The diversity of the FGF protein family is irrelevant to Applicants' assertion of utility

The Action asserts that because it is well recognized in the art that the FGF family of proteins is complex and diverse and that the members of this family exhibit a broad range of biological activities involving cell growth and differentiation, the specification does not describe a substantial utility for any of the claimed sequences. Specifically, the Action states that the prior art of record demonstrates that the FGF family of proteins is so diverse that one of ordinary skill in the art could not predict which biological activity a particular protein possesses merely by classifying that protein as a member of the family.

Although the family of FGF proteins may be diverse, Applicants respectfully disagree with the Action's assertion that as a result of this diversity, the instant specification does not describe a substantial utility for any of the claimed FGF-like nucleic acid molecules. Applicants contend, instead, that because their assertion of utility rests on *more* than the structural similarity of the claimed nucleic acid molecules to members of the FGF family (as described above), one of ordinary skill in the art would readily recognize that the as-filed specification asserts a substantial utility for the claimed sequences. It is Applicants' belief that the Action focuses too much attention on the *name* Applicants use to describe their novel sequences, and too little attention on the *actual experimental results* Applicants describe in their specification.

i. The instant situation is not analogous to that addressed in *Brenner v. Manson*

The Action asserts that the issue of utility presented by the instant application is directly analogous to the issue of utility addressed in *Brenner v. Manson*, 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

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Applicants respectfully disagree with the Action's assertion the utility issues presented in *Brenner* and the instant application are *directly* analogous. In *Brenner*, the Supreme Court determined that claims to a chemical *process* (and *not* the chemicals themselves) for producing steroids belonging to a particular class of steroids (said class of steroids comprising one known member previously proven effective in inhibiting tumors in mice) lacked patentable utility because the applicants had not disclosed a sufficient likelihood that the steroids produced by the claimed process had similar tumor-inhibiting properties. As stated in *Brenner*, those applicants disclosed nothing more than (a) a process for producing steroids, and (b) that the compounds produced by the claimed process were homologues of a single known compound shown to have tumor-inhibiting properties. The Court's rationale was that excluding others from making, selling, and, most importantly, using the claimed methods would extend patent protection to the undisclosed and unknown compounds. The instant claims are different in almost every way. First, they are composition of matter claims, so there is no similar global inhibition of technological progress as was present in *Brenner*. Second, the instant application affirmatively teaches specific nucleic acid molecules encoding polypeptides that were found to be actually *expressed* in animals, primarily in the liver. Third, overexpression of these polypeptides in transgenic mice produces an inhibited or delayed maturation phenotype, including, for example, reduced body weight and reduced liver weight as a percent of body weight. Applicants contend, therefore, that the instant application provides the public with a specific benefit (*i.e.*, a particular member of the FGF family – and the first FGF shown to be expressed primarily in the liver, which is associated with a specific function). This situation is *wholly unlike* the circumstances in *Brenner*, where the chemical process of *Brenner* produced a class of compounds which might *not* have been produced in nature and which might have had *no* useful function whatsoever. Under these circumstances, the pending claims do not improperly "engross what may prove to be a broad field." *Brenner*, 383 U.S. at 534-35.

Applicants respectfully contend that one of ordinary skill in the art would recognize that the as-filed specification asserts a substantial utility for the claimed sequences, and therefore, request that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 101.

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2. **Rejections of claims 1(c)-(e), 2-5, 7-13, and 39-43 under 35 U.S.C. § 112, first paragraph**

a. Rejection of claims 1(c)-(e), 2-5, 7-13, 39-43 under the written description requirement of 35 U.S.C. § 112, first paragraph

The Office Action maintains the rejection of claims 1(c)-(e), 2-5, 7-13, 39-43 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully disagree with the Action's assertion that claimed invention has not been adequately described, and address each of the Action's individual assertions as to this ground of rejection below.

i. Claim 1(c)

The Action asserts that the written description is insufficient to support the numerous nucleotide sequences recited in claim 1(c), wherein the potential biological activity and primary sequence of the polypeptides encoded by the recited nucleotide sequences are not necessarily the same as that of SEQ ID NO: 4.

Applicants respectfully disagree with the Action's assertion that the nucleotide sequences recited in claim 1(c) are not adequately described. Claim 1(c) recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4. In other words, claim 1(c) defines a genus of degenerate nucleotide sequences encoding either the polypeptide set forth in SEQ ID NO: 2 or the polypeptide set forth in SEQ ID NO: 4. Applicants contend that each member of the genus of nucleotide sequences defined by claim 1(c) must encode a polypeptide possessing the primary sequence set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, and therefore, must possess the biological activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4. Moreover, Applicants contend that in view of the recognized degeneracy of the genetic code, one of ordinary skill in the art could readily envision the detailed structure of *not just* a representative number of species of the genus of molecules defined by claim 1(c), but rather, of *every single* member of that genus.

Furthermore, Applicants contend that the Action provides no support for the assertion that the description of an amino acid sequence (such as that provided in the instant specification in SEQ ID

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NO: 2 and SEQ ID NO: 4) is insufficient to support a claim to degenerate nucleotide sequences encoding the disclosed amino acid sequence. Applicants contend that in view of the explicitly-disclosed sequences provided by the instant application, one of ordinary skill in the art could readily determine the structure of nucleic acid molecules encoding the polypeptides set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, and would recognize that Applicants were in possession of the claimed invention. Applicants, therefore, submit that claim 1(c) satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

ii. Claim 1(d)

The Action also asserts that the as-filed specification does not meet the written description requirement for claiming a genus of nucleotide sequences that hybridize under at least moderately stringent conditions to the nucleotide sequences recited in claims 1(a) to 1(c), and which must exhibit any of the activities contemplated by the as-filed specification, wherein such activities are in conflict with one another.

Applicants respectfully disagree with the Action's assertion that the nucleotide sequences recited in claim 1(d) are not adequately described. Claim 1(d), as amended, recites an isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of any of claims 1(a) to 1(c) at 50°C in a hybridization buffer comprising 0.015 M NaCl, 0.0015 M sodium citrate, and 0.1% SDS. Applicants note that the Federal Circuit has recently indicated that a claim which recites a genus of nucleotide sequences based on their hybridization properties "may be adequately described if [the claimed nucleic acid molecules] hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1327 (Fed. Circ. 2002). Applicants also note that the instant specification describes hybridization at 50°C in a buffer comprising 0.015 M NaCl, 0.0015 M sodium citrate, and 0.1% SDS as "highly stringent" (*see, e.g.*, page 10, lines 3-5). Applicants submit that in view of the explicitly-disclosed sequences and highly stringent hybridization conditions provided by the instant application, claim 1(d) satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

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iii. Claim 1(e)

The Action maintains the written description rejection as to claim 1(e), asserting that this claim reads on nucleotide sequences that do not necessarily encode the polypeptide of SEQ ID NO: 4, but which must exhibit one of the activities contemplated by the as-filed specification.

Applicants respectfully disagree with the Action's assertion that the nucleotide sequences recited in claim 1(e) are not adequately described. Claim 1(e) recites an isolated nucleic acid molecule comprising a nucleotide sequence that is complementary to the nucleotide sequence of any of claims 1(a) to 1(d). Because claim 1(e) recites a genus of nucleotide sequences that are *complementary* to the nucleotide sequences defined in claims 1(a) to 1(d), Applicants do not disagree with the Action's assertion that the nucleotide sequences recited in claim 1(e) would *not* encode the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4. Applicants, however, do not understand how such an assertion is relevant to the issue of whether claim 1(e) complies with the written description requirement since claim 1(e) does note recite that the claimed nucleic acid molecules would encode the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4. Moreover, Applicants contend that in view of the recognized ability of nucleic acid molecules to associate by basepairing, one of ordinary skill in the art could readily envision the detailed structure of *not just* a representative number of species of the genus of molecules defined by claim 1(e), but rather, of *every single* member of that genus.

Furthermore, Applicants contend that the Action provides no support for the assertion that the description of a nucleotide sequence (such as that provided in the instant specification in SEQ ID NO: 1 and SEQ ID NO: 3) is insufficient to support a claim to nucleotide sequences that are complementary to the described sequence. Applicants, on the other hand, note that the Federal Circuit has recently indicated that "[g]iven the sequence of a single strand of DNA or RNA, it may have become a routine matter to envision the precise sequence of a 'complementary' strand that will bind to it," and therefore, "disclosure of a DNA sequence might support a claim to the complementary molecules that can hybridize to it." *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 925 (Fed. Circ. 2004). Applicants contend that one of ordinary skill in the art could readily determine the structure of nucleic acid molecules that are complementary to the nucleotide

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sequences defined in claims 1(a) to 1(d) and would recognize that Applicants were in possession of the claimed invention. Applicants, therefore, submit that claim 1(e) satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

iv. Claim 39

The Action maintains the written description rejection as to claim 39, asserting that this claim reads on nucleotide sequences that do not necessarily encode the polypeptide of SEQ ID NO: 4, but which must exhibit one of the activities contemplated by the as-filed specification.

Applicants respectfully disagree with the Action's assertion that the nucleotide sequences recited in claim 39 are not adequately described. Claim 39 recites an isolated nucleic acid molecule comprising a region of the nucleotide sequence of either SEQ ID NO: 1 or SEQ ID NO: 3 or the DNA insert in ATCC Deposit No. PTA-626, encoding a polypeptide fragment of at least about 25 amino acid residues; a region of the nucleotide sequence of either SEQ ID NO: 1 or SEQ ID NO: 3 or the DNA insert in ATCC Deposit No. PTA-626 comprising a fragment of at least about 16 nucleotides; or a nucleotide sequence that is complementary to the above nucleotide sequences. Applicants contend that because the specification explicitly teaches the amino acid sequence for murine and human FGF-like polypeptide (Figures 1 and 2A-2B), the specification inherently discloses fragments of murine and human FGF-like polypeptide, since fragments are merely portions of the specifically disclosed full-length murine and human FGF-like polypeptide sequences.

Furthermore, Applicants contend that the Action provides no support for the assertion that the description of a nucleotide sequence (such as that provided in the instant specification in SEQ ID NO: 1 and SEQ ID NO: 3) is insufficient to support a claim to fragments of that sequence. Applicants contend that in view of the explicitly-disclosed sequences provided by the instant application, one of ordinary skill in the art could readily determine the structure of nucleic acid molecules encoding fragments of the polypeptide of SEQ ID NO: 1 or SEQ ID NO: 3 or the polypeptide encoded by the DNA insert of ATCC Deposit No. PTA-626, and would recognize that Applicants were in possession of the claimed invention Applicants, therefore, submit that claim 39 satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

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v. Claim 40

The Action maintains the written description rejection as to claim 40, asserting that this claim reads on nucleotide sequences that do not necessarily encode the polypeptide of SEQ ID NO: 4, but which must exhibit one of the activities contemplated by the as-filed specification.

Although Applicants respectfully disagree with the Action's assertion that the nucleotide sequences recited in claim 40 are not adequately described, Applicants have cancelled this claim in an effort to expedite prosecution of the pending claims to allowance, rendering this ground of rejection moot. Applicants reserve the right to pursue claims directed to nucleic acid molecules encoding FGF-like polypeptide substitution variants in a timely filed continuation or divisional application.

Applicants respectfully contend that rejections based on the written description requirement of 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

b. Rejection of claims 1(c)-(e), 2-5, 7-13, 39-43 under the enablement requirement of 35 U.S.C. § 112, first paragraph

The Office Action also maintains the rejection of claims 1(c)-(e), 2-5, 7-13, and 39-43 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. Applicants respectfully disagree with the Action's assertion that the instant specification does not enable the claimed invention, and address each of the Action's individual assertions as to this ground of rejection below.

i. Claims 1(c)-(e), 2, 5, 8, 9, 13, and 42

The Action asserts that while the specification is enabling for the nucleotide sequences recited in claims 1(a), 1(b), 39, and 40, the as-filed specification does not provide sufficient guidance or evidentiary support to reasonably enable the broad scope of claims 1(c)-(e), 2, 5, 8, 9, 13, and 42, without resorting to undue experimentation. Specifically, the Action states that because the members

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of the FGF family display a broad range of biological activities, and it is well-recognized in the art that a protein's function cannot be determined from structural similarity *alone*, the specification fails to teach the skilled artisan how to make and use the claimed nucleic acid molecules, other than those recited in claims 1(a), 1(b), 39, and 40, without resorting to undue experimentation.

Applicants respectfully disagree with the Action's assertion that claims 1(c)-(e), 2, 5, 8, 9, 13, and 42 are not enabled. As described in section 2(a)(i) above, claim 1(c) recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 (*i.e.*, degenerate nucleotide sequences that encode the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4). In contrast, claim 1(a), which the Action states is enabled, recites an isolated nucleic acid molecule comprising a nucleotide sequence as set forth in either SEQ ID NO: 1 or SEQ ID NO: 3 (*i.e.*, nucleotide sequences that encode the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4, respectively). Applicants contend that because each member of the genus of nucleotide sequences defined by claim 1(c) must encode a polypeptide possessing the primary sequence set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, and therefore, the biological activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 4, one of ordinary skill in the art could readily make and use the nucleotide sequences encompassed by claim 1(c). In other words, if the nucleotide sequences of 1(a) are enabled, as the Action states, then the nucleotide sequences of claim 1(c) must likewise be enabled.

As described in section 2(a)(ii) above, claim 1(d) recites an isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of any of claims 1(a) to 1(c) at 50°C in a hybridization buffer comprising 0.015 M NaCl, 0.0015 M sodium citrate, and 0.1% SDS. Applicants contend that because one of ordinary skill in the art could readily determine whether a particular nucleotide sequence is encompassed by claim 1(d) by hybridizing the nucleotide sequence to the complement of one of the nucleotide sequences recited in claims 1(a)-(c) at 50°C in a hybridization buffer comprising 0.015 M NaCl, 0.0015 M sodium citrate, and 0.1% SDS, the genus of nucleotide sequences recited in claim 1(d) is enabled.

As described in section 2(a)(iii), claim 1(e) recites an isolated nucleic acid molecule comprising a nucleotide sequence that is complementary to the nucleotide sequence of any of claims 1(a) to 1(d). Applicants contend that in view of the recognized ability of nucleic acid molecules to

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associate by basepairing, one of ordinary skill in the art could readily make the nucleotide sequences defined by claim 1(e). In addition, Applicants contend that one of ordinary skill in the art would recognize that the nucleotide sequences encompassed by claim 1(e) could be used, for example, as probes for detecting murine or human FGF-like transcripts in a cell. Applicants, therefore, contend that the genus of nucleotide sequences recited in claim 1(e) is enabled.

In addition, Applicants respectfully disagree with the Action's assertion that the ascribed function of the disclosed FGF-like polypeptides rests *only* on their structural similarity to members of the FGF family, as discussed more fully in section 1 above. Applicants briefly reiterate that the specification discloses, at page 4, lines 22-28, that 6-8 week old transgenic mice overexpressing an FGF-like transgene exhibit an abnormal phenotype generally characterized as inhibited or delayed maturation, including reduced body weight, reduced liver weight as a percent of body weight, reduced spleen weight as percent of body weight, increased thymic weight as percent of body weight, and poorly developed ovaries with lack of significant follicular development. Applicants contend, therefore, that they have affirmatively supplied a specific biological function for polypeptides encoded by the claimed nucleic acid molecules, and that the function of the disclosed polypeptides thus rests on *more* than their structural similarity to members of the FGF family.

ii. Claims 2 and 9-11

The Action asserts that claims 2 and 9-11 are not enabled because they embrace "any host cell comprising any of [the] DNAs encoding a FGF-like polypeptide," and further, because claims 2 and 9-11 as written are not necessarily limited to cultured or isolated host cells, and therefore, it is not apparent how one of ordinary skill in the art could prepare non-isolated or cultured cells as broadly claimed.

Applicants respectfully disagree with the Action's assertion that claims 2 and 9-11 are not enabled because they embrace "any host cell comprising any of [the] DNAs encoding a FGF-like polypeptide." Applicants note that claim 2 recites "[a] recombinant host cell comprising a nucleic acid molecule comprising the nucleotide sequence of any of Claims 1, 39, or 40." Applicants also note that claim 9 recites "[a] recombinant host cell comprising the vector of Claim 8," and that claim 8, in turn, recites "[a] vector comprising the nucleic acid molecule of Claims 1, 39, or 40."

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Applicants further note that the specification *explicitly* defines the term "FGF-like polypeptides" as encompassing the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4, *as well as* polypeptides encoded by allelic variants of the nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 3, polypeptides encoded by splice variants of the nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 3; fragments of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; derivatives of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; substitution variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; deletion variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; insertion variants variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; fusion polypeptides variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; and orthologs of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4 (page 11, lines 20-27). Because amended claims 1, 39, and 40 *clearly do not* encompass nucleotide sequences encoding *all* of the FGF-like polypeptides contemplated by the as-filed specification, claims 2 and 9-11, which depend from claims 1, 39, and 40, *clearly cannot* encompass recombinant host cells comprising nucleotide sequences encoding *any* FGF-like polypeptide. In other words, claims 2 and 9-11 do not even encompass host cells comprising nucleotide sequences encoding *all* of the FGF-like polypeptides contemplated by the as-filed specification, let alone host cells comprising nucleotide sequences encoding *any* FGF-like polypeptide.

Applicants also disagree with the Action's assertion that claims 2 and 9-11 are not enabled because these claims as written are not necessarily limited to cultured or isolated host cells. Applicants note that claims 2 and 9, as previously presented, recite "[a] recombinant host cell." In addition, Applicants have amended claims 10 and 11 to refer to the *recombinant* host cell of claim 9. Applicants contend that one of ordinary skill in the art would readily understand that the term "recombinant host cell" refers to a cultured or isolated host cell (*see, e.g.*, claims 11-13 of U.S. Patent No. 6,723,534, issued April 20, 2004). Applicants, therefore, contend that claims 2 and 9-11 satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

iii. Claim 5 and 42

The Action asserts that claims 5 and 42 are not enabled because these claims embrace a

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method of producing "any FGF-like polypeptide recombinantly," and it is not apparent as to how a skilled artisan could employ the recited host cells to express any FGF-like polypeptide.

Applicants respectfully disagree with the Action's assertion that claims 5 and 42 are not enabled because they encompass a process of producing *any* FGF-like polypeptide. Applicants note that claims 5 and 42 have been amended to recite "[a] process of producing a polypeptide encoded by the nucleic acid molecule of any of Claims 1, 39, or 40." As described in section 2(b)(ii) above, the specification *explicitly* defines the term "FGF-like polypeptides" as encompassing the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4, *as well as* polypeptides encoded by allelic variants of the nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 3, polypeptides encoded by splice variants of the nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 3; fragments of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; derivatives of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; substitution variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; deletion variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; insertion variants variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; fusion polypeptides variants of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4; and orthologs of the polypeptides set forth in SEQ ID NO: 2 and SEQ ID NO: 4 (page 11, lines 20-27). Because amended claims 1, 39, and 40 *clearly do not* encompass nucleotide sequences encoding *all* of the FGF-like polypeptides contemplated by the as-filed specification, claims 5 and 42, which depend from claims 1, 39, and 40, *clearly cannot* encompass processes of producing *any* FGF-like polypeptide. In other words, claims 5 and 42 do not even encompass processes of producing *all* of the FGF-like polypeptides contemplated by the as-filed specification, let alone *any* FGF-like polypeptide. Applicants contend that claims 5 and 42, as amended, do not encompass processes of producing *any* FGF-like polypeptide, but rather encompass processes of producing a polypeptide encoded by the nucleotide sequences of claims 1, 39, or 40, and therefore, that these claims satisfy the enablement requirement.

iv. Claim 12

The Action asserts that claim 12 is not reasonably enabled on the basis of the specification and the state of the art, since it would require undue experimentation for one of ordinary skill in the

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art to determine which of the activities contemplated by the as-filed specification a compound inhibited.

Applicants respectfully disagree with the Action's assertion that claim 12 is not reasonably enabled because the specification does not disclose or provide evidentiary support for a specific biological activity of the disclosed polypeptides. As discussed in section 1 above, the instant application explicitly teaches that 6-8 week old transgenic mice overexpressing an FGF-like transgene exhibit an abnormal phenotype generally characterized as inhibited or delayed maturation, including reduced body weight, reduced liver weight as a percent of body weight, reduced spleen weight as percent of body weight, increased thymic weight as percent of body weight, and poorly developed ovaries with lack of significant follicular development (page 4, lines 22-28). Thus, one of ordinary skill in the art would recognize that compounds that inhibit FGF-like peptide activity would antagonize this phenotype. Nevertheless, in an effort to expedite prosecution of the pending claims to allowance, Applicants have amended this claim to recite a process for determining whether a compound inhibits FGF-like polypeptide *production* comprising exposing a cell according to Claim 2 to the compound, and measuring FGF-like polypeptide production in said cell. Applicants contend that claim 12, as amended, is enabled. Applicants reserve the right to pursue claims directed to processes for determining whether a compound inhibits FGF-like polypeptide activity in a timely filed continuation or divisional application.

Applicants respectfully contend that rejections based on the enablement requirement of 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Nguyen believes it to be helpful, he is invited to contact the undersigned representative by telephone at 312-913-0001.

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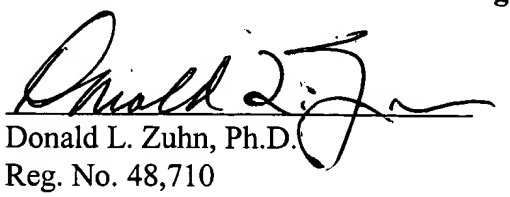
Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: July 6, 2004

By: 
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